Unlocking the Full Potential of the Immune System Against Cancer

Corporate Presentation

January 23, 2024

Disclaimer

This presentation contains forward-looking statements, which are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated. There can be no guarantee that (i) the results of pre-clinical work and prior clinical trials will be predictive of the results of the clinical trials currently under way, (ii) regulatory authorities will agree with the Company's further development plans for its therapies, or (iii) the Company will find development and commercialization partners for its therapies in a timely manner and on satisfactory terms and conditions, if at all. The occurrence of any of these risks could have a significant negative outcome for the Company's activities, perspectives, financial situation, results and development.

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Innovative Clinical-Stage Immunotherapy Portfolio Based on Viral Vectors

Cutting-edge **individualized neoantigen cancer vaccine** (TG4050)

- **Proof of principle in randomized Phase I study** (H&N adjuvant)
- Randomized Phase II trial to start in 2024

Additional **immuno-oncology programs** with **clinical proof of principle**

- **Shared antigens vaccines (HPV16)**
- **Oncolytic viruses**

Significant value creation catalysts expected in **2024**

TG4050 – A Novel Individualized Cancer Immunotherapy

MVA VECTOR BENEFITS

- Induces **broad and specific immune response** – 100% patients treated develop a polyepitopic response*
  - *Strongly differentiated from mRNAs and peptides*
- Excellent safety profile
- Proven immunogenicity in challenging immune contexture

THE RIGHT NEOANTIGENS

- Comprises **up to 30 neoantigens** selected using NEC's artificial intelligence and machine learning

Orchestrating a brighter world
NEC

INDICATION

- Targeting head and neck patients – **designed to prevent relapse**
- Only neoantigen cancer vaccine targeting this indication in adjuvant situation
- Potential to address other indications in perioperative setting

myvac

Building upon proof of concept:

Randomized Phase II trial to begin in 2024

based on promising Phase I data

*Source: Ottensmeier et al, " Safety and Immunogenicity of TG4050: a personalized cancer vaccine in head and neck carcinoma" ASCO 2023, June 6, 2023, Poster presentation

Focus on Neoantigen Cancer Vaccine
While Delivering Proof of Principles on a Diversified Immunotherapy Portfolio

Product	Indication	Collaboration	Discovery	Phase I	Phase II	Key upcoming catalysts
INDIVIDUALIZED NEOANTIGEN CANCER VACCINES						
TG4050 myvac	Head and neck cancer (adjuvant)	Orchestrating a brighter world NEC	●	●	●	**Additional immunogenicity and follow up data on Ph. I trial (H1 2024) – 24-month median follow up (H2 2024)**
	Other indication		●	●		**Ph. II trial in head and neck cancers to start (2024)** Additional Ph. I trial to start (2025)
SHARED ANTIGENS CANCER VACCINES						
TG4001	Anogenital HPV+ cancers		●	●	●	**Randomized Phase II trial results (H2 2024)**
Internal myvac	Shared driver mutations		●			
ONCOLYTIC VIRUSES (OVs)						
TG6050 invir io	Lung cancer (IV*)		●	●		Phase I trial completion (H2 2024)
BT-001 invir io	Solid tumors (IT*)	BioInvent	●	●		Complete enrolment (H1 2024) and first data in combination with pembrolizumab (H2 2024)
Internal	Synthetic OV (IV*)		●			

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** IV: intravenous administration, IT: Intratumoral administration*

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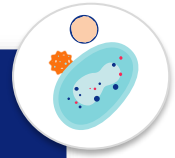
Cancer Therapeutic Vaccines

Focused on delivering the promise
of individualized cancer vaccine

myvac® - TG4050 | Combines Unique Know How and Expertise

MVA viral vector: a powerful platform for vaccine development



Strongly immunogenic vector

- Demonstrated capability to express **complex antigen structures** and have them presented by APCs
- Ability to elicit **strong, durable and specific** immune response
- Established safety profile

Optimal neoantigen display

- **VacDesignR™** for **optimal design of the recombinant cassettes**
- Selection of **best promoter sequences**

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one patient • one genome • one vaccine

Artificial Intelligence to identify up to 30 potent neoantigens

- NEC's machine learning environment based on multiple parameters **to classify most immunogenic neoantigens** from whole tumor genome analysis*
  - **Takes in account multiple parameters**
- **NEC covers 50% of the clinical development costs of TG4050**

NEC

Technology well suited to demonstrate benefit in minimal residual/molecular disease

Click here

AACR American Association for Cancer Research

*Source: Mallone et al., "Performance of neoantigen prediction for the design of TG4050, a patient-specific neoantigen cancer vaccine", AACR, June 2020, Poster presentation

TG4050 | HPV-Negative Head and Neck Cancer - Trial after Surgery and Adjuvant Therapy

Surgery +
Adjuvant
chemoradiotherapy

Complete
Clinical Response (approx. 90%)
RANDOMIZATION

myvac
TG4050
(single agent)
Repeated injections

Patient monitoring
(no treatment)

LEAD INVESTIGATOR: Pr. Christian Ottensmeier,
Clatterbridge Cancer Care Center, Liverpool

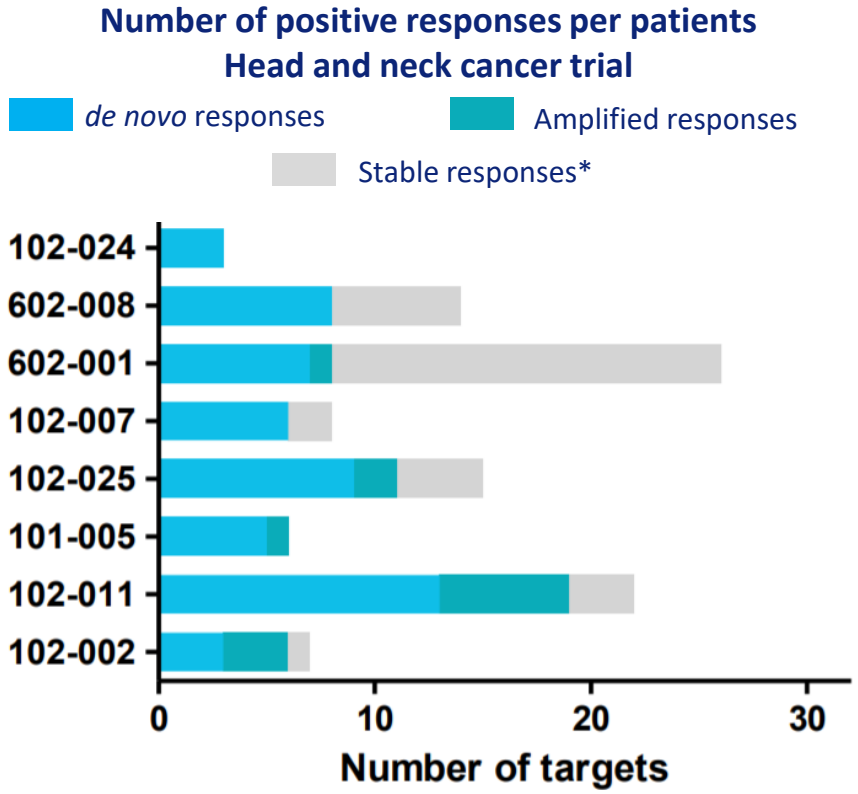
Need to prevent or delay relapse
Clinical situation where checkpoint blockers have failed (ie. KN412, Javelin 100)
24-month PFS remains approx. 60%*

Randomized Phase I trial – Promising initial immunological and clinical data presented at ASCO 2023
32 patients (NCT: 04183166)

- ➔ **All treated patients remaining disease-free**
- ➔ **Additional immunological data and clinical update expected in H1 2024**
- ➔ **24-month median follow up expected in H2 2024**
- ➔ **Trial extended to Phase I/II, patient inclusions to restart in 2024**

* Source: Keynote 412, Javelin 100 trials

TG4050 | Generates an Unprecedented Rate of T Cell Response Against Tumor Specific Epitopes



Induction of multiple T cell responses in all treated patients

Profound remodeling of immune cells consistent with anti tumor response

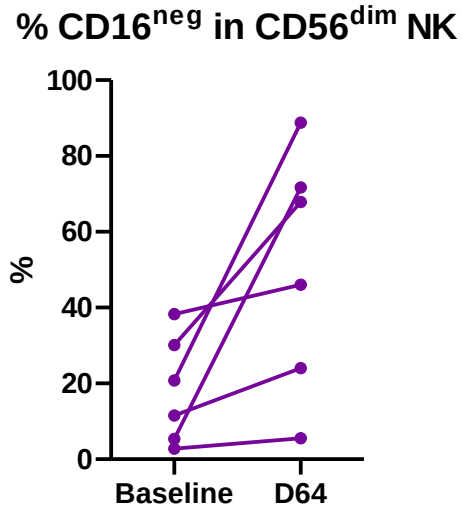
**Immunoreactive T-cells present at baseline but not amplified by vaccine*

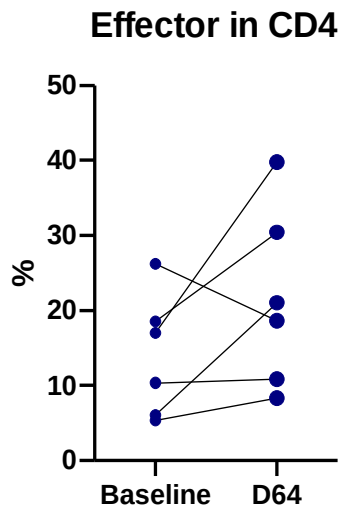
2023 ASCO ANNUAL MEETING

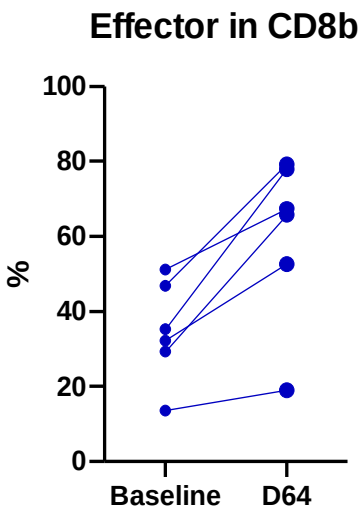
Source: Ottensmeier et al, " Safety and Immunogenicity of TG4050: a personalized cancer vaccine in head and neck carcinoma" ASCO 2023, June 6, 2023, Poster presentation

Profound Remodelling of Immune Cells Consistent with Anti Tumor Response

Suggests that the Vaccine Effectively Primes the Immune System







- **Priming of innate immunity**: Loss of CD16 on $CD56^{dim}$ NK cells suggests **ongoing antitumor activity**
- **Maturation and differentiation of CD4 and CD8 into effector cells** – Consistent with the development of an active adaptive response
- **Effector subgroups of CD4 and CD8 T-cells are increased**

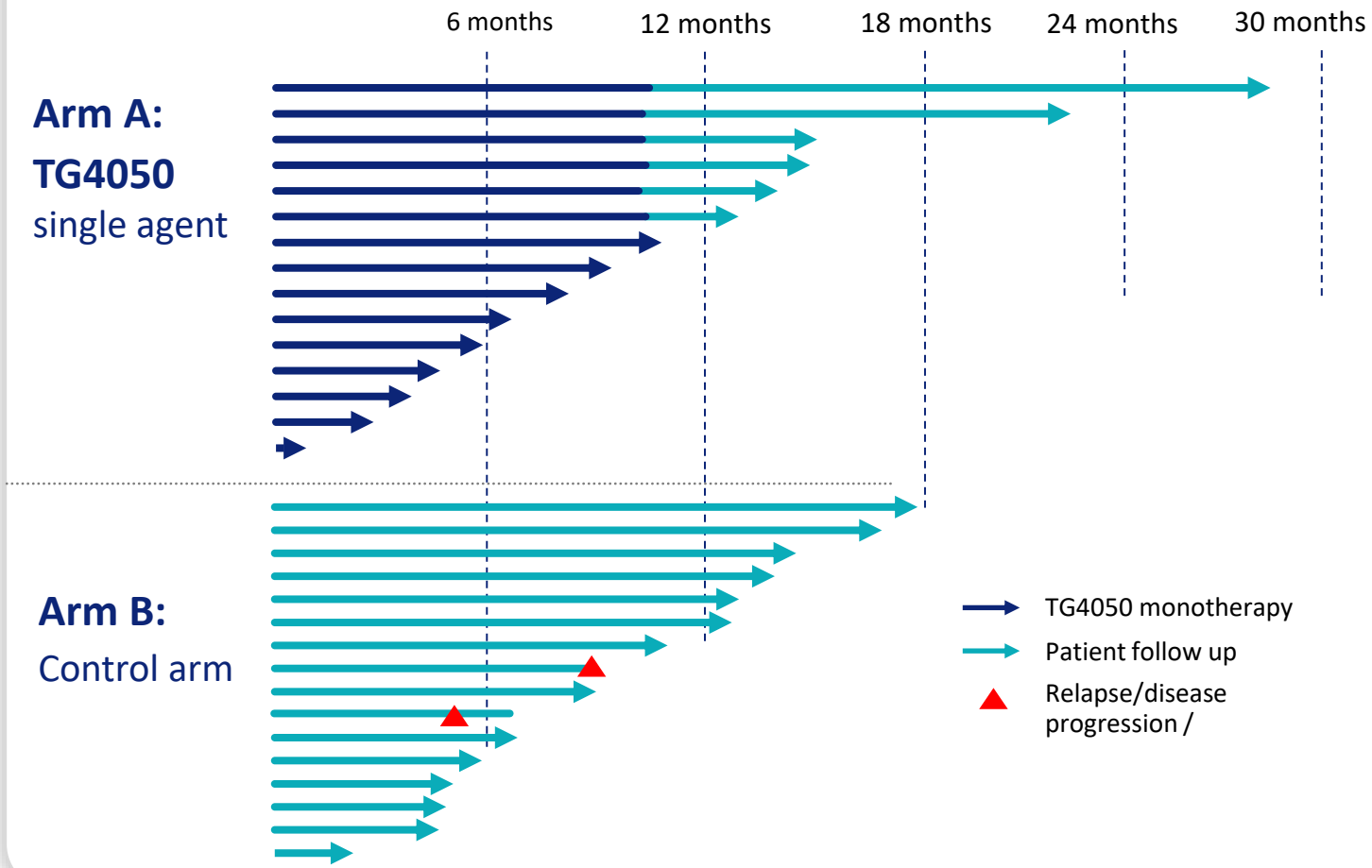
AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

Source: Block et al, "Phase I trials of personalized cancer vaccine TG4050 in surgically treated high-risk head and neck squamous cell carcinoma (HNSCC) and relapsing ovarian cancer (OvC) patients" AACR 2022, April 12, 2022, Poster presentation

Promising First Signals of Clinical Activity in Adjuvant Setting

Head & Neck Cancer Trial

32 patients randomized – May 2023



No related SAEs
Good safety profile

All 16 treated patients were disease-free

Only patients in the control arm relapsed

Trial fully enrolled

2023 ASCO ANNUAL MEETING

Source: Ottensmeier et al, " Safety and Immunogenicity of TG4050: a personalized cancer vaccine in head and neck carcinoma" ASCO 2023, June 6, 2023, Poster presentation

TG4050 | Building upon Proof of Concept with a Randomized Phase II Trial

Mid-term objective: Establish TG4050 as the SOC in adjuvant setting for patients with H&N cancers

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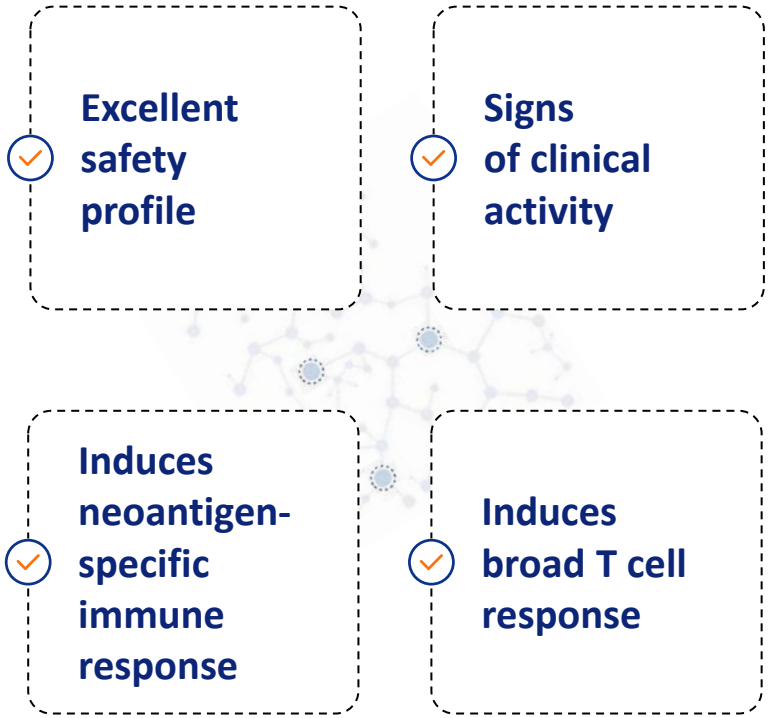
one patient • one genome • one vaccine



- Intend to launch randomized **Phase II trial in head and neck cancers** in 2024 – Additional immunological data and Ph. I trial update in **H1 2024 – 24-month median follow up expected in H2 2024**
- **Potential to extend remission period and address a significant market** (head and neck cancer – adjuvant)
- **Potential to address other solid tumors in perioperative settings w or w/o ICIs**, such as urothelial, breast, lung cancers – Additional trial to start in 2025

TG4001 | Proof of Concept Data Expected in H2 2024 – Seeking Partnership in 2024

Ongoing Phase II trial in patients with HPV16-positive anogenital cancer

incl. cervical, vulvar, vaginal, penile and anal cancers
NCT: 03260023

Patients with recurrent / metastatic disease

Randomized (1:1)

- **TG4001 + avelumab**
- **Avelumab single agent**

Treated in 1st line or in 2nd line (with a maximum of 1 prior systemic chemotherapy)

Without liver metastasis at baseline

Without previous exposure to cancer immunotherapy

Including all levels of PD-L1 expression

Clinical collaboration with MERCK for avelumab free supply

Ongoing trial to readout in H2 2024

- To deliver PoC data in significant patient population
- To further validate MVA platform

Clear path to approval in recently changed landscape

- Phase III in 1st line HPV+ cervix cancer in combin. with SoC (CT + ICI)
- Pivotal 2nd line after ICI

Objective

Sign partnership or licensing agreement based on Ph. II data

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Oncolytic Viruses

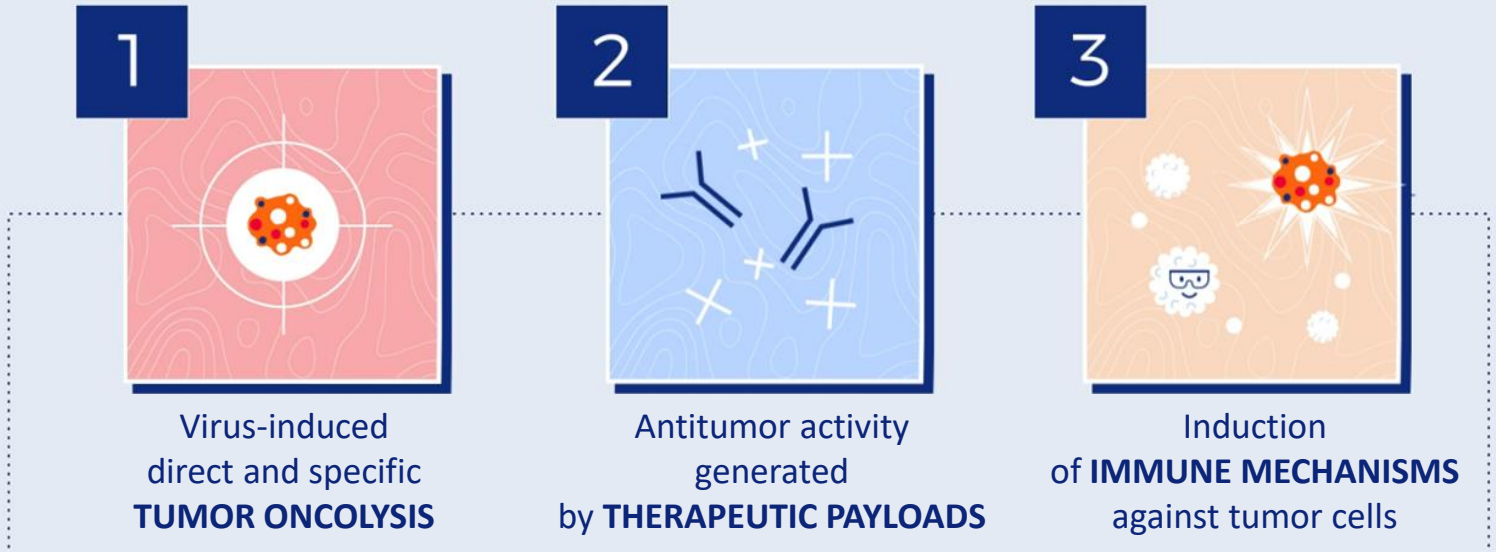
Rapidly Generating Multiple Virus-Powered
Off-the-Shelf Drug Candidates Targeting Solid Tumors

invir io

Our Oncolytic Viruses (OV) – Combined Effects of Vector, Payload and Immune Stimulation

Compelling Clinical Data Support Intravenous (IV) Route of Administration

Cancer cell death through multiple MOAs



Patented Backbone VVcopTK-RR- vector with multiple competitive advantages

- ➜Encode numerous and various **payloads**
- ➜**Multiple routes of administration** (IV, IT, locoregional) and extend OV market beyond IT administration
- ➜Potential to target multiorgan lesions and warm up TME
- ➜Address broad range of solid tumors

invir io

Proof of principle obtained

- Good safety profile
- Able to reach tumors, selectively replicate and express payload, incl. via **intravenous administration**

Goal: to target multiorgan lesions and reverse tumor resistance

TG6050 administered IV | IL-12 and anti-CTLA4 Produced Directly in the Tumor

Ongoing Phase I Trial to Assess Systemic Route of Administration

Oncolytic armed with IL-12 and anti-CTLA4 Ab

- Triggers a powerful antitumor immune response
- Restores the immune defenses within the tumor

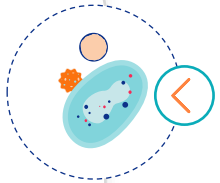
The Invir.IO® objective

- Avoid toxicity / off target thanks to selective replication of viral vector
- Ensure sufficient production of IL-12 in the tumor
- **Outstanding preclinical data (strong antitumor activity) presented at AACR 2023**

Phase I trial - Indication: metastatic and PD1 failed tumors

- Advanced or metastatic NSCLC after failure with available treatment options, including anti-PD1/PD-L1 – **Intravenous (IV) administration**
- Inclusions ongoing (NCT: 05788926)
- Phase I trial completion (single agent) in H2 2024 – Could be combined with ICIs

Potential to address a major oncology market



Initial goal

demonstrate potential of IV administration in “cold”, non-resectable metastatic tumors

AACR ANNUAL MEETING 2023

Source: Marchand et al, TG6050, “An oncolytic vaccinia virus armed with interleukin 12 and anti-CTLA4 antibody induces TME remodeling and strong anti-tumoral responses” AACR 2023, April 16, 2023, Poster presentation

BT-001 | OV Armed with Anti-CTLA4 Ab + GM-CSF

Ongoing Phase I Trial Assessing IT* Route of Administration

50/50 collaboration with **BioInvent**

The right virus + payload

$VV_{cop}TK^{-}RR^{-}$ oncolytic armed with BioInvent's potent **anti-CTLA4 Ab** + **GM-CSF**

· Activates and increases T-effector cells
· Treg depleting activity
· Stimulates immune cells (incl. APC)

Winner of the **2022 JITC Best Oncolytic** and Local Immunotherapy Paper **Award**

Can be developed for multiple cancer indications

lesions with high Treg infiltration

Positive Phase I part A readout

- Single agent **well tolerated**
- **Replicates** and **persists** **in tumor tissue**
- **Anti-CTLA4 expressed in the tumor** with **no detectable systemic exposure**
- **Stable injected lesion** in **11/18 patients**
- **Tumor shrinkage** observed in two patients

Ongoing Phase I (NCT04725331)

monotherapy and combination w. anti-PD1

- **Ph. I part B** (combination with pembrolizumab) – Enrolment ongoing (Expected completion in H1 2024) – First data expected in H2 2024

Collaboration with MSD
which provides pembrolizumab (KEYTRUDA®)

**IT: intratumoral administration*

Outlook

Company Funded to Deliver Multiple Value Generating Milestones

FINANCIAL VISIBILITY
until **end of 2024**

Ownership

As of September 30, 2023

- Listed on Euronext Paris
- ISIN: FR0005175080 - Ticker: TNG

2024 Value Creating News Flow Expected in Next 12 Months

TG4050

Proof of principle

already obtained in head and neck cancer (adjuvant)

Ongoing randomized Phase I

- Additional immunogenicity and clinical follow up data (H1 2024)
- 24-month median follow up of patients (H2 2024)

Phase II

- Initiation of the trial in collaboration with NEC

Other indication

- Prepare new Phase I

TG4001 - Results from ongoing randomized Phase II (H2 2024)

TG6050 - Phase I data (H2 2024)

BT-001 - Inclusion of the last patient in the Phase IB study of BT-001 (H1 2024)

Investment Highlights

Unique and highly potent viral vector based immunotherapies

Lead program TG4050 to deliver data in 2024 and create significant value by 2026

Additional programs and R&I activity to deliver news flow and fuel Transgene's portfolio in the mid term

Appendices

New Leadership to Take Transgene to the Next Level

ALESSANDRO RIVA, MD
Chairman & CEO

30+ years experience

NOVARTIS ONCOLOGY GILEAD ...ichnos...

ÉRIC QUÉMÉNEUR, PharmD, PhD - Executive VP - Chief Scientific Officer

MAUD BRANDELY, MD, PhD - VP, Medical Affairs - Chief Medical Officer

CHRISTOPHE ANCEL, PharmD
VP, Pharmaceutical Operations

ARNAUD DUBARRY
VP, Chief Financial Officer

JOHN FELITTI
VP, Legal Counsel

LUCIE LARGUIER
VP, Communication & IR

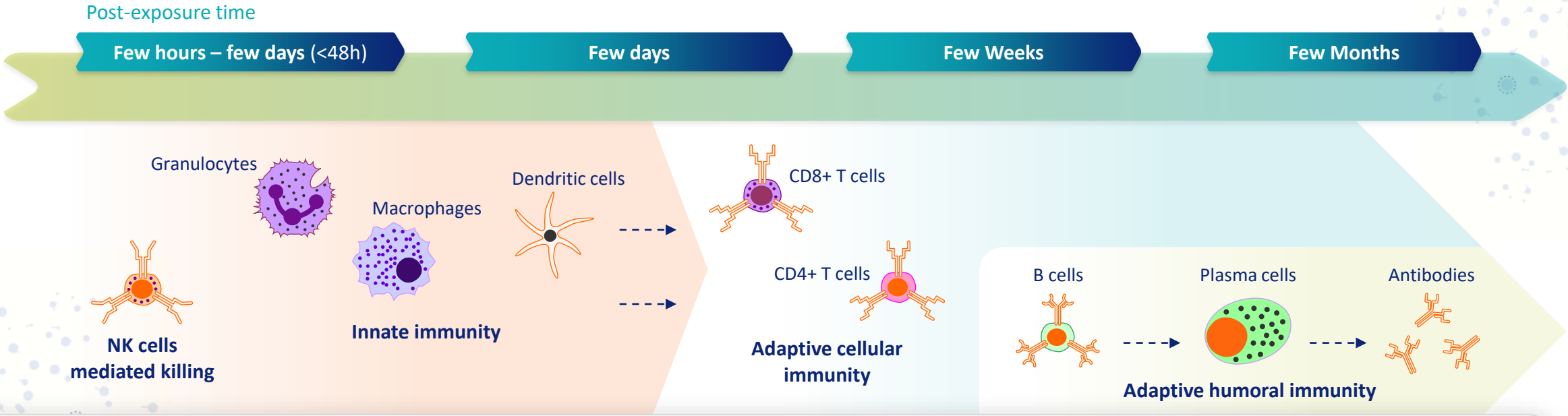
GAELLE STADTLER
VP, Human Resources

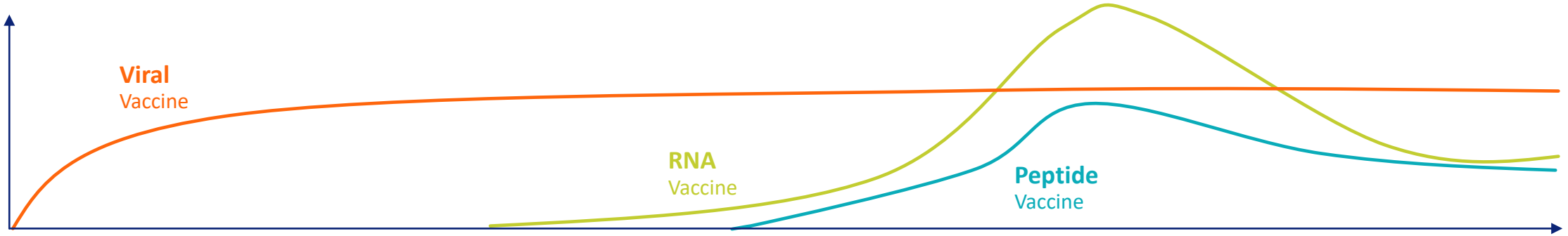
JAMES WENTWORTH
VP, Chief Business Officer

JOHN C. BELL
Member of the Scientific Advisory Board

PEDRO ROMERO
Member of the Scientific Advisory Board

Viral Vaccines Prime Both Long Lasting Innate and Adaptive Immunity





Sources: Karinko K et al. Immunity, 2005; Collier ARY et al. NEJM, 2021

TG4050, an Individualized Neoantigen Vaccine Combining Unique Capabilities

Combines Bioengineering and Digital Transformation

ROUTINE TUMOR BIOPSY

Patient

STANDARD GENE/EXOME SEQUENCING

Next generation sequencing

DATA PROCESSING, ARTIFICIAL INTELLIGENCE

Selection of 30 neoantigens

GENE EDITING

Vaccine generation VacDesignR™

GMP MANUFACTURING

Production of the individual batch

TREATMENT ADMINISTRATION

Patient

Sequencing Lab

Orchestrating a brighter world NEC

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